

FOR RELEASE: Tuesday, May 7, 2002

Media contact: Paul Preuss, (510) 486-6249, paul_preuss@lbl.gov

Science contact: Michael Banda, (510) 495-2837, MJBanda@lbl.gov

A FIRST LINE OF DEFENSE AGAINST DISEASE ORGANISMS
Joint Genome Institute to Sequence Infectious
Bacteria

WALNUT CREEK, CALIF. — The Department of Energy's Joint Genome Institute (JGI), whose Production Genome Facility in Walnut Creek is one of the fastest and most powerful in the U.S., has been enlisted to help safeguard public safety by determining the whole genome sequences of a variety of infectious bacteria—a first step toward developing tests that can be used to rapidly identify their presence in the environment.

While the anthrax strains used in recent bioterrorist attacks could be identified, there are no field tests for dozens of other potentially dangerous microbes. To develop new tests and improve existing ones, knowing the whole genomic sequence of each organism and its close relatives can be vitally important.

JGI is ideally suited to this effort because of its capacity and depth of experience in sequencing microorganisms. In a little over three years JGI has sequenced scores of microbes; last year it sequenced 15 bacteria in a single month and today is capable of sequencing an average microbe's genome twice over in a single day.

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Starting Tuesday (May 7), JGI's Production Genomics Facility will determine draft genome sequences of several bacteria already under study at Lawrence Livermore and Los Alamos national laboratories. JGI was founded in 1997 by these two laboratories and Lawrence Berkeley National Laboratory; all three laboratories are managed for the Department of Energy by the University of California.

The first pathogens to be sequenced under the current program are members of the *Bacillus*, *Brucella*, *Clostridium*, *Francisella*, *Shigella*, and *Yersinia* groups. In many of these groups, several strains or related species will be sequenced, for example, two strains of *Bacillus anthracis* (anthrax) and one of the similar species *Bacillus thuringiensis*.

Depending on how quickly the organisms become available, JGI plans to sequence the whole genomes of many more potentially hazardous bacteria and a number of their less harmful relatives.

Sequencing at JGI will not involve actual pathogens. Whole organisms will be received and handled at laboratories equipped with appropriate containment facilities, like those in place at Livermore and Los Alamos, where the DNA of each pathogen will be reduced to fragments to be sent in a disassembled state to JGI's Production Genomics Facility.

The genome of a typical bacterium is a circular piece of DNA containing approximately two to five million "base pairs"—pairs of the chemical bases, integral to the DNA molecule, that form the letters of the genetic code. Genomes from millions of individual bacteria are fragmented to create a library of random pieces each about two to three thousand base pairs long. Each fragment represents only about 0.0005 percent of the complete genome.

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Because intact genomes are not involved, the Centers for Disease Control and Prevention have registered the PGF to receive this fragmentary DNA with no change in standard procedures. The PGF will work with multiple copies of each fragment. Automated equipment determines the exact sequence of bases on each strand. The data is then assembled by a computer program to reconstruct the order of the bases in the whole genome.

The completed sequence exists only as a string of letters in a computer's output. No physical genomes will be handled at JGI, and the standard laboratory strain of *E. coli* in which individual DNA fragments are reproduced will be disposed of after sterilization, according to the standard operating procedures of the PGF. Draft sequences will be shared with Los Alamos and Lawrence Livermore laboratories for finishing and annotation.

JGI has been a leader in sequencing organisms of crucial interest to researchers around the world. For the Human Genome Project, JGI sequenced human chromosomes 5, 16, and 19, which together constitute some 11 percent of the human genome. JGI sequenced mouse DNA related to human chromosome 19 to illuminate the molecular evolutionary history of the two species. Working with an international consortium of universities and industry, JGI participated in the sequencing of the gene-rich puffer fish (*Fugu rubripes*). The 165-million base-pair genome of the sea squirt (*Ciona intestinalis*) was sequenced jointly by JGI, Japan's National Institute of Genetics, and Kyoto University. JGI has also sequenced the environmentally important white rot fungus (*Phanerochaete chrysosporium*) and over 50 important microorganisms.

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The Joint Genome Institute is one of the largest publicly funded human genome sequencing institutions in the world. With its main headquarters and Production Genomics Facility in Walnut Creek, JGI employs about 240 people and has programs in genomic sequencing, computation, functional genomics, genomic diversity, and new technology development. Funding is provided predominantly by the Department of Energy's Office of Science; other agencies that have contributed to funding JGI include DOE's National Nuclear Security Administration, the National Institutes of Health, the National Science Foundation, and the U.S. Department of Agriculture.

More information about the Joint Genome Institute can be found at www.jgi.doe.gov online.